REMARKS

Please cancel claims 1-14 without disclaimer or prejudice. Please enter new claims 15-38. Support for new claims 15-37 can be found throughout the specification. For Example support for claims 15-17 is found at page 92, lines 1-15; support for claim 18 can be found at page 7, lines 23-24; support for claim 19 can be found at page 25, line 2; support for claim 20 can be found at page 28, line30, page 29, lines 1-6 and page 56, lines 21-22; support for claim 21 can be found at page 97, lines 24-25; support for claim 22 can be found at page 112, lines 21-30; support for claim 24 can be found at page 56, lines 21-22; support for claims 26-27 can be found at page 92, lines 1-15; support for claims 29-32 can be found at page 8, lines 15-23 and page 6, lines 12-18; and support for claims 35-37 can be found at page 7, lines 23-24. Therefore no new subject matter is added and entry of the amendment is respectfully requested. For the Examiner's convenience, a clean copy of all pending claims is attached, entitled "**Appendix A: Pending Claims**". Also attached for the Examiner's convenience is a version showing changes made. In addition to the claim amendments , enclosed herein are substitute drawings in compliance with 37 CFR § 1.84.

VERSION SHOWING CHANGES MADE

Claims 1-14 are canceled.

15.(new) A method of genotyping an allele of a target nucleic acid sequence comprising:

a) providing a target nucleic acid sequence comprising a first domain and a second domain, wherein said first and said second domains are separated by a detection position;

b) forming a first hybridization complex by:

i) hybridizing a first primer comprising an adapter sequence to said first domain, immediately adjacent to and 3' of said detection position;

ii) hybridizing a second primer to said second domain, immediately adjacent to and 5' of said detection position;

c) contacting said first hybridization complex with dNTPs and a first enzyme to form a modified hybridization complex;

d) contacting said modified hybridization complex with a second enzyme to form a ligated probe; and

e) detecting the presence of said ligated probe.

16.(new) The method according to claim 15, wherein said first enzyme is a polymerase.

17.(new) The method according to claim 15, wherein said second enzyme is a ligase.

18.(new) The method according to claim 15, wherein said dNTPs comprise a label.

19.(new) The method according to claim 18 wherein said label is a fluorescent label.

20.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with an array comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first subpopulation comprising a first capture probe, such that said first capture probe and said ligated probe comprising said adapter sequence to form a second hybridization complex; wherein said microspheres are distributed on said surface; and

g) detecting the presence of said second hybridization complex.

21.(new) The method according to claim 20, wherein said substrate is a fiber optic bundle.

22.(new) The method according to claim 20, wherein said substrate is selected form the group consisting of glass and plastic.

23.(new) The method according to claim 20, wherein said discrete sites comprise wells.

24.(new) The method according to claim 15 wherein said second primer further comprises an adapter sequence.

25.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with an ordered array , wherein said ordered array comprises capture probes.

26.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with a population of microspheres comprising at least a first subpopulation comprising a first capture probe, such that said first capture probe and said ligated probe comprising said adapter sequence form a second hybridization complex.

27.(new) A method comprising:

a. providing a hybridization complex comprising:

i) a target nucleic acid comprising a first and a second domain separated by a detection position;

ii) a first probe hybridized to said first domain, wherein said first probe further comprises an adapter sequence that is not complementary to said target sequence; and

iii) a second probe hybridized to said second domain;

b. contacting said hybridization complex with nucleotides and an extension enzyme such that said first probe is extended to form an extended first probe comprising a nucleotide that is complementary to said detection position, whereby a modified hybridization complex is formed;

c. contacting said modified hybridization complex with a ligase, whereby said extended first probe and said second probe are ligated forming a ligated probe; and

d) detecting said ligated probe.

28.(new) The method according to claim 27, wherein said detecting comprises:

contacting said ligated probe with a first immobilized capture probe, whereby said adapter hybridizes with said capture probe.

29.(new) The method according to claim 28,wherein said capture probe is immobilized on an ordered array.

30.(new) The method according to claim 28, wherein said capture probe is immobilized on a first population of microspheres.

31.(new) The method according to claim 28, wherein said capture probe is immobilized on a first population of microspheres, wherein said microspheres are randomly distributed on a substrate.

32.(new) The method according to claim 31, wherein said substrate is a fiber optic bundle.

33.(new) The method according to claim 27, wherein said substrate is selected from the group consisting of glass and plastic.

34.(new) The method according to claim 27 wherein said nucleotides are dNTPS

35.(new) The method according to claim 34, wherein said dNTPs are labeled

36.(new) The method according to claim 27, wherein said second probe comprises a label.

37.(new) The method according to claim 27, wherein said extension enzyme is a DNA polymerase.

IN THE SPECIFICATION

Delete paragraph at page 1, lines 3-4 following the title and replace with the following re-written paragraph:

---- This application claims benefit of U.S. Application Serial Number 60/244,119, filed October 26, 2000, which is expressly incorporated herein by reference.--

Appendix A: Pending Claims

15.(new) A method of genotyping an allele of a target nucleic acid sequence comprising:

a) providing a target nucleic acid sequence comprising a first domain and a second domain, wherein said first and said second domains are separated by a detection position;

b) forming a first hybridization complex by:

i) hybridizing a first primer comprising an adapter sequence to said first domain, immediately adjacent to and 3' of said detection position;

ii) hybridizing a second primer to said second domain, immediately adjacent to and 5' of said detection position;

c) contacting said first hybridization complex with dNTPs and a first enzyme to form a modified hybridization complex;

d) contacting said modified hybridization complex with a second enzyme to form a ligated probe; and

e) detecting the presence of said ligated probe.

16.(new) The method according to claim 15, wherein said first enzyme is a polymerase.

17.(new) The method according to claim 15, wherein said second enzyme is a ligase.

18.(new) The method according to claim 15, wherein said dNTPs comprise a label.

19.(new) The method according to claim 18 wherein said label is a fluorescent label.

20.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with an array comprising:

i) a substrate with a surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first subpopulation comprising a first capture probe, such that said first capture probe and said ligated probe comprising said adapter sequence to form a second hybridization complex; wherein said microspheres are distributed on said surface; and

g) detecting the presence of said second hybridization complex.

21.(new) The method according to claim 20, wherein said substrate is a fiber optic bundle.

22.(new) The method according to claim 20, wherein said substrate is selected form the group consisting of glass and plastic.

23.(new) The method according to claim 20, wherein said discrete sites comprise wells.

24.(new) The method according to claim 15 wherein said second primer further comprises an adapter sequence.

25.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with an ordered array , wherein said ordered array comprises capture probes.

26.(new) The method according to claim 15 further comprising:

f) contacting said ligated probe with a population of microspheres comprising at least a first subpopulation comprising a first capture probe, such that said first capture probe and said ligated probe comprising said adapter sequence form a second hybridization complex.

27.(new) A method comprising:

a. providing a hybridization complex comprising:

i) a target nucleic acid comprising a first and a second domain separated by a detection position;

ii) a first probe hybridized to said first domain, wherein said first probe further comprises an adapter sequence that is not complementary to said target sequence; and

iii) a second probe hybridized to said second domain;

b. contacting said hybridization complex with nucleotides and an extension enzyme such that said first probe is extended to form an extended first probe comprising a nucleotide that is complementary to said detection position, whereby a modified hybridization complex is formed;

c. contacting said modified hybridization complex with a ligase, whereby said extended first probe and said second probe are ligated forming a ligated probe; and

d) detecting said ligated probe.

28.(new) The method according to claim 27, wherein said detecting comprises:

contacting said ligated probe with a first immobilized capture probe, whereby said adapter hybridizes with said capture probe.

29.(new) The method according to claim 28,wherein said capture probe is immobilized on an ordered array.

30.(new) The method according to claim 28, wherein said capture probe is immobilized on a first population of microspheres.

31.(new) The method according to claim 28, wherein said capture probe is immobilized on a first population of microspheres, wherein said microspheres are randomly distributed on a substrate.

32.(new) The method according to claim 31, wherein said substrate is a fiber optic bundle.

33.(new) The method according to claim 27, wherein said substrate is selected from the group consisting of glass and plastic.

34.(new) The method according to claim 27 wherein said nucleotides are dNTPS

35.(new) The method according to claim 34, wherein said dNTPs are labeled

36.(new) The method according to claim 27, wherein said second probe comprises a label.

37.(new) The method according to claim 27, wherein said extension enzyme is a DNA polymerase.

CONCLUSION

Applicants submit the claims are in condition for allowance, and early notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,
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